REMARKS/ARGUMENTS

Claims 4, 5, 9, and 10 are pending. Claims 4 and 5 are under active consideration. Claims 9 and 10 are withdrawn from consideration.

The objection to Claim 5 is believed to be obviated by the amendment submitted above. That claim has been amended to specify that the nucleoside 5'-phosphate ester is selected from the group consisting of inosine 5'-phosphate ester and guanosine 5'-phosphate ester. Accordingly, withdrawal of this objection is respectfully requested.

The rejection of Claims 4 and 5 under 35 U.S.C. §112, second paragraph, is respectfully traversed.

Claim 4 reads as follows:

> An isolated bacterium belonging to the genus Escherichia having an ability to produce and accumulate nucleoside 5'-phosphate ester in a medium, wherein the ushA gene and the aphA gene of the bacterium are disrupted.

Applicants submit that Claim 4 is definite. The claim recites that the bacterium belongs to the genus Escherichia and has an ability to produce and accumulate nucleoside 5'-phosphate ester in a medium. The claim also specifies that the ushA gene and the aphA gene of the bacteria are disrupted. One reading Claim 4 will readily appreciate the metes and bounds of the subject matter embraced by the claim.

In addition, in order to show that Escherichia bacteria other than E. coli also have ushA and aphA genes which have high homology to thus genes from E. coli, printouts from the DDBJ, which indicate the genes of the following accession Nos., are submitted herewith:

Accession NO. AE000154: ushA gene from E. coli K12

Accession NO. AF068226: ushA gene from Enterobacter aerogenes

Accession NO. AE015074: ushA gene from Shigella flexneri

Accession NO. AE000479. aphA gene from E. coli K12

Accession NO. AE015424: aphA gene from Shigella flexneri

Accession NO. AE008898: aphA gene from Salmonella typhimurium

From the printouts, it is clear that, in spite of the different genera to which the bacteria belong, the ushA genes and aphA genes of the bacteria have high homology with respect to each other. Therefore, a bacterium which belongs to the same genus to which E. coli belongs (i.e., the genus Escherichia), is expected to have ushA genes and aphA genes that are highly homologous to the genes of E. coli.

In addition, the printouts show that even ushA genes and aphA genes from a bacterium which belongs to a genus other than Escherichia are also called as "ushA gene" or "aphA gene," just like in E. coli.

In view of the foregoing, Claims 4 and 5 are definite within the meaning of 35 U.S.C. §112, second paragraph. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 4 and 5 under 35 U.S.C. §102(b) over Laird is respectfully traversed. That reference fails to describe the claimed bacterium.

In the 54G2 strain described by Laird, the purEK gene is disrupted in addition to the ushA and aphA genes. The purEK gene encodes for 5-phosphoribosyl-5-aminoimidazole carboxylase, which is involved in purine biosynthesis. The disruption of purEK gene imparts a purine requirement to the strain. Therefore, the 54G2 strain of Laird cannot produce nucleoside 5'-phosphate esters such as inosine 5'-phosphate ester, which is produced via the purine synthesis pathway. On the other hand, the claimed bacterium has the ability to produce and accumulate nucleoside 5'-phosphate esters such as inosine 5'-phosphate ester. Therefore, the bacterium of the present claims 4-5 is different from the bacterium of Laird.

Furthermore, Laird does not disclose or suggest that disrupting both ushA gene and aphA gene causes an accumulation of nucleoside 5'-phosphate ester in the medium.

Therefore, Claims 4-5 are patentable over Laird. Withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 4 and 5 under 35 U.S.C. §103(a) over Thaller alone or in view of Cowman is respectfully traversed. Those references fail to suggest the claimed bacterium.

Thaller describes the sequence of the aphA gene from E. coli, and characterizes the product of that gene as a 5'-nucleoside (see the Abstract). The reference speculates that "the AphA enzyme could represent a physiological equivalent of the periplasmic 5'-nucleotidase (UshA)" (see page 197, column 1). Thaller also suggests that genetically defined aphA mutations may be useful to understand the physiological role of the enzyme and the significance of the enzymatic activity "under laboratory conditions" (see page 198, first column). The reference fails to describe bacteria in which the ushA gene or the aphA gene are disrupted, or even suggest that such bacteria would have the ability to produce and accumulate nucleoside 5'-phosphate ester in a medium.

Cowman teaches the ushA gene from E. coli encoding a 5'-nucleotidase. The reference fails to describe bacteria in which the ushA gene or the aphA gene are disrupted, or even suggest that such bacteria would have the ability to produce and accumulate nucleoside 5'-phosphate ester in a medium.

One skilled in the art would not have expected that disrupting the ushA gene and aphA gene in a bacterium belonging to the genus Escherichia would produce a bacterium which accumulates nucleoside 5'-phosphate ester in the medium.

Generally, a bacterium has about 6 types of 5'-nucleotidases. In order to exemplify such a bacterium, Document 1 (J Biochem., 83, 409-421 (1978)) is submitted herewith. Document 1 shows that Bacillus subtilis has 7 types of 5'-nucleotidases (See Table V). It had been expected that E. coli also has about 6 types of 5'-nucleotidases. On the contrary to this

expectation, E. coli has only two types of 5'-nucleotidases (AshA and UshA), which was demonstrated by the inventor of the present invention (See Table 5 and page 32 lines 4-6 of the present specification).

In addition, when either the ushA gene or the aphA gene was disrupted, i.e., only one of the two genes was disrupted, IMP (inosine 5'-phosphate ester) was not accumulated in the medium (ushA mutant, 0g; aphA mutant, 0g; see Table 6 of the present specification). On the other hand, when both the ushA gene and the aphA gene were disrupted, 0.8 g/L of IMP was on average accumulated in the medium (See Table 6 of the present specification).

These results demonstrate that both the ushA gene or the aphA gene must be disrupted in order to produce a bacterium which has an ability to produce and accumulate nucleoside 5'-phosphate ester in a medium. It is not sufficient to disrupt only one of the genes. That result could not be predicted from Thaller and Cowman, each alone or taken in combination. Neither reference even describes a disrupted ushA gene or aphA gene. Therefore, one with these references in hand would not have been able to predict that it would be necessary to disrupt both the ushA gene and the aphA gene in order to produce a bacterium which has an ability to produce and accumulate nucleoside 5'-phosphate ester in a medium.

Based on the foregoing, Claims 4 and 5 are not obvious over Thaller and Cowman considered alone or in combination. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Applicants note the Restriction Requirement. However, Claims 9 and 10 depend from the elected claims. Therefore, upon the allowance of Claims 4 and 5, Claims 9 and 10 should be rejoined with the elected claims. See MPEP §821.04 at page 800-63, Revised Eight Edition, February 2003.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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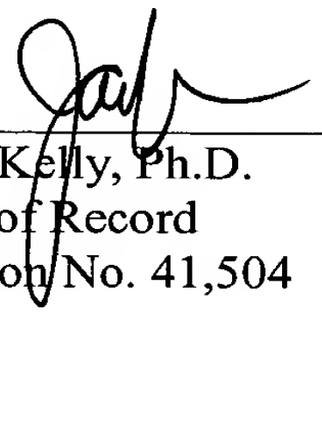

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IN THE CLAIMS

Please amend the claims as follows:

Claims 1-3 (Canceled).

Claim 4 (Twice Amended): An isolated bacterium belonging to the genus Escherichia having an ability to produce and accumulate nucleoside 5'-phosphate ester in a medium, wherein the ~~in which~~ ushA gene and the aphA gene of the bacterium are disrupted.

Claim 5 (Twice Amended): The isolated bacterium belonging to the genus Escherichia according to Claim 4, wherein the nucleoside 5'-phosphate ester is selected from the group consisting of inosine 5'-phosphate ester and guanosine 5'-phosphate ester ~~5'-inosinic acid or 5'-guanylic acid~~.

Claims 6-8 (Canceled).

Claim 9 (Previously Presented): A method for producing a nucleoside 5'-phosphate ester comprising, culturing the isolated bacterium of Claim 4 in a medium to produce and accumulate the nucleoside 5'-phosphate ester in the medium; and collecting the nucleoside 5'-phosphate ester from the medium.

Claim 10 (Previously Presented): A method for producing a nucleoside 5'-phosphate ester comprising, culturing the isolated bacterium of Claim 5 in a medium to produce and accumulate the nucleoside 5'-phosphate ester in the medium; and collecting the nucleoside 5'-phosphate ester from the medium.

SUPPORT FOR THE AMENDMENTS

Claim 4 has been amended for clarity. Claim 5 has been amended to specify that the nucleoside 5'-phosphate ester is selected from the group consisting of inosine 5'-phosphate ester and guanosine 5'-phosphate ester. No new matter is believed to have been added to this application by that amendment.